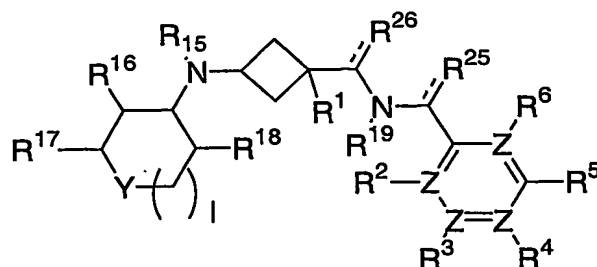


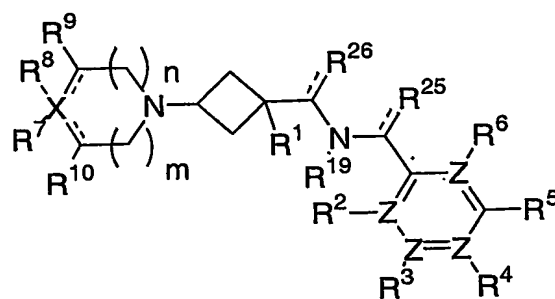
WHAT IS CLAIMED IS:

1. A compound of formula I or formula II:



I

5



II

10 wherein:

X is O, N, S, SO₂ or C;

15 Y is selected from: -O-, -NR¹²-, -S-, -SO-, -SO₂-, and -CR¹²R¹²-, -NSO₂R¹⁴-,
-NCOR¹³-, -CR¹²COR¹¹-, -CR¹²OCOR¹³- and -CO-;

20 R¹¹ is selected from: hydroxy, hydrogen, C₁-6alkyl, -O-C₁-6alkyl, benzyl, phenyl and C₃-6cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents, and where said substituents are independently selected from: halo, hydroxy, C₁-3alkyl, C₁-3alkoxy, -CO₂H, -CO₂-C₁-6alkyl and trifluoromethyl;

5 R^{12} is selected from: hydrogen, C₁₋₆ alkyl, benzyl, phenyl and C₃₋₆cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents, and where said substituents are independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆alkyl, and trifluoromethyl;

10 R^{13} is selected from: hydrogen, C₁₋₆alkyl, -O-C₁₋₆alkyl, benzyl, phenyl and C₃₋₆cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents, and where said substituents are independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆alkyl and trifluoromethyl;

15 R^{14} is selected from: hydroxy, C₁₋₆ alkyl, -O-C₁₋₆alkyl, benzyl, phenyl, C₃₋₆cycloalkyl, where said alkyl, phenyl, benzyl and cycloalkyl groups are unsubstituted or substituted with 1-3 substituents, and where said substituents are independently selected from: halo, hydroxy, C₁₋₃alkyl, C₁₋₃alkoxy, -CO₂H, -CO₂-C₁₋₆ alkyl and trifluoromethyl;

20 each Z is independently selected from C or N, where at most two of the Z are N;

R^1 is selected from:
(a) hydrogen,
(b) -C₁₋₆alkyl,
(c) -C₀₋₆alkyl-O-C₁₋₆alkyl,
25 (d) -C₀₋₆alkyl-S-C₁₋₆alkyl,
(e) -(C₀₋₆alkyl)-(C₃₋₇cycloalkyl)-(C₀₋₆alkyl),
(f) hydroxy,
(g) heterocycle,
(h) -CN,
30 (i) -NR¹²R¹²,
(j) -NR¹²COR¹³,
(k) -NR¹²SO₂R¹⁴,
(l) -COR¹¹,
(m) -CONR¹²R¹², and
35 (n) phenyl;

40 where said alkyl and cycloalkyl are unsubstituted or substituted with 1-7 substituents, and where said substituents are independently selected from: halo, hydroxy, -O-C₁₋₃alkyl, trifluoromethyl, C₁₋₃alkyl, -O-C₁₋₃alkyl, -COR¹¹, -SO₂R¹⁴, -NHCOCH₃, -NHSO₂CH₃, -heterocycle, =O, -CN, and

where said phenyl and heterocycle are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -COR¹¹, C₁-3alkyl, C₁-3alkoxy and trifluoromethyl;

5 R² is selected from:

- (a) hydrogen,
- (b) C₁-3alkyl, optionally substituted with 1-3 fluoro,
- (c) -O-C₁-3alkyl, optionally substituted with 1-3 fluoro,
- 10 (d) hydroxy,
- (e) chloro,
- (f) fluoro,
- (g) bromo,
- (h) phenyl,
- 15 (i) heterocycle, and
- (j) nothing or O (when the Z bonded to R² is N);

R³ is selected from:

- 20 (a) hydrogen,
- (b) C₁-3alkyl, optionally substituted with 1-3 fluoro,
- (c) -O-C₁-3alkyl, optionally substituted with 1-3 fluoro,
- (d) hydroxy,
- (e) chloro,
- 25 (f) fluoro,
- (g) bromo,
- (h) phenyl,
- (i) heterocycle, and
- (j) nothing or O (when the Z bonded to R³ is N);

30

R⁴ is selected from:

- (a) hydrogen,
- (b) C₁-3alkyl, optionally substituted with 1-3 fluoro,
- 35 (c) -O-C₁-3alkyl, optionally substituted with 1-3 fluoro,
- (d) hydroxy,
- (e) chloro,
- (f) fluoro,
- (g) bromo,
- 40 (h) phenyl,
- (i) heterocycle, and
- (j) nothing or O (when the Z bonded to R⁴ is N);

R⁵ is selected from:

- 5 (a) C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro and optionally substituted with hydroxyl,
- (b) -O-C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (c) -CO-C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- 10 (d) -S-C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (e) -pyridyl, which is unsubstituted or substituted with one or more substituents selected from: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹,
- 15 (f) fluoro,
- (g) chloro,
- (h) bromo,
- (i) -C₄₋₆cycloalkyl,
- (j) -O-C₄₋₆cycloalkyl,
- 20 (k) phenyl, which is unsubstituted or substituted with one or more substituents selected from: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹,
- (l) -O-phenyl, which is unsubstituted or substituted with one or more substituents selected from: halo, trifluoromethyl, C₁₋₄alkyl, and COR¹¹,
- 25 (m) -C₃₋₆cycloalkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- (n) -O-C₃₋₆cycloalkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
- 30 (o) -heterocycle,
- (p) -CN, and
- (q) -COR¹¹;

R⁶ is selected from:

- 35 (a) hydrogen,
- (b) C₁₋₃alkyl, optionally substituted with 1-3 fluoro,
- (c) -O-C₁₋₃alkyl, optionally substituted with 1-3 fluoro,
- (d) hydroxy,
- 40 (e) chloro,
- (f) fluoro,
- (g) bromo,

- (h) phenyl,
- (g) heterocycle, and
- (h) nothing, when the Z bonded to R⁶ is N;

5 R⁷ is selected from:

- (a) hydrogen,
- (b) (C₀₋₆alkyl)-phenyl,
- (c) (C₀₋₆alkyl)-heterocycle,
- (d) (C₀₋₆alkyl)-C₃₋₇cycloalkyl,
- 10 (e) (C₀₋₆alkyl)-COR¹¹,
- (f) (C₀₋₆alkyl)-(alkene)-COR¹¹,
- (g) (C₀₋₆alkyl)-SO₃H,
- (h) (C₀₋₆alkyl)-W-C₀₋₄alkyl,
- (i) (C₀₋₆alkyl)-CONR¹²-phenyl,
- 15 (j)(C₀₋₆alkyl)-CONR²⁰-V-COR¹¹, and
- (k) nothing, when X is O, S, or SO₂),

where W is selected from: a single bond, -O-, -S-, -SO-, -SO₂-, -CO-, -CO₂-, -CONR¹²- and -NR¹²-, where V is selected from C₁₋₆alkyl or phenyl,

20

where R²⁰ is hydrogen, C₁₋₄alkyl or is joined via a 1-5 carbon tether to one of the carbons of V to form a ring, where the C₀₋₆alkyl is unsubstituted or substituted with 1-5 substituents,

25

where said substituents are independently selected from: halo, hydroxy, -C₀₋₆alkyl, -O-C₁₋₃alkyl, trifluoromethyl, and -C₀₋₂alkyl-phenyl,

30

where the phenyl, heterocycle, cycloalkyl, and C₀₋₄alkyl is unsubstituted or substituted with 1-5 substituents where the substituents are independently selected from: halo, trifluoromethyl, hydroxy, C₁₋₃alkyl, -O-C₁₋₃alkyl, -C₀₋₃-COR¹¹, -CN, -NR¹²R¹², -CONR¹²R¹², and -C₀₋₃-heterocycle, or where the phenyl and heterocycle are fused to another heterocycle, which itself is unsubstituted or substituted with 1-2 substituents independently selected from hydroxy, halo, -COR¹¹, and -C₁₋₃alkyl,

35

and where alkene is unsubstituted or substituted with 1-3 substituents which are independently selected from: halo, trifluoromethyl, C₁₋₃alkyl, phenyl, and heterocycle;

40 R⁸ is selected from:

- (a) hydrogen,
 (b) nothing when X is either O, S, SO₂ or N or when a double bond joins
 the carbons to which R⁷ and R¹⁰ are attached,
 (c) hydroxy,
 5 (d) C₁₋₆alkyl,
 (e) C₁₋₆alkyl-hydroxy,
 (f) -O-C₁₋₃alkyl,
 (g) -COR¹¹,
 (h) -CONR¹²R¹², and
 10 (i) -CN;

or where R⁷ and R⁸ are be joined together to form a ring which is selected from:

- (a) 1H-indene,
 15 (b) 2,3-dihydro-1H-indene,
 (c) 2,3-dihydro-benzofuran,
 (d) 1,3-dihydro-isobenzofuran,
 (e) 2,3-dihydro-benzothiofuran,
 (f) 1,3-dihydro-isobenzothiofuran,
 20 (g) 6H-cyclopenta[d]isoxazol-3-ol
 (h) cyclopentane, and
 (i) cyclohexane,

25 where the ring formed is unsubstituted or substituted with 1-5 substituents
 independently selected from: halo, trifluoromethyl, hydroxy, C₁₋₃alkyl, -O-
 C₁₋₃alkyl, -C₀₋₃-COR¹¹, -CN, -NR¹²R¹², -CONR¹²R¹², and -C₀₋₃-
 heterocycle,

30 or where R⁷ and R⁹ or R⁸ and R¹⁰ are joined together to form a ring which is phenyl
 or heterocycle, where said ring is unsubstituted or substituted with 1-7 substituents,
 where said substituents are independently selected from: halo, trifluoromethyl,
 hydroxy, C₁₋₃alkyl, -O-C₁₋₃alkyl, -COR¹¹, -CN, -NR¹²R¹², and -CONR¹²R¹²;

35 R⁹ and R¹⁰ are independently selected from:

- (a) hydrogen,
 (b) hydroxy,
 (c) C₁₋₆alkyl,
 (d) C₁₋₆alkyl-COR¹¹,
 40 (e) C₁₋₆alkyl-hydroxy,
 (f) -O-C₁₋₃alkyl,
 (g) =O, when R⁹ or R¹⁰ is connected to the ring via a double bond, and

(h) halo;

R¹⁵ is hydrogen or C₁₋₆alkyl, which is unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo,
5 hydroxy, -CO₂H, -CO₂C₁₋₆alkyl, and -O-C₁₋₃alkyl;

R¹⁶ is selected from:

- (a) hydrogen,
- 10 (b) C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 substituents where the substituents are selected from: fluoro, C₁₋₃alkoxy, hydroxy, -COR¹¹,
- (c) fluoro,
- (d) -O-C₁₋₃alkyl, where alkyl is unsubstituted or substituted with 1-3
15 fluoro, and
- (e) C₃₋₆ cycloalkyl,
- (f) -O-C₃₋₆cycloalkyl,
- (g) hydroxy,
- (h) -COR¹¹,
- 20 (i) -OCOR¹³,

or R¹⁵ and R¹⁶ are joined together via a C₂₋₄alkyl or a C₀₋₂alkyl-O-C₁₋₃alkyl chain to form a 5-7 membered ring;

25 R¹⁷ is selected from:

- (a) hydrogen,
- (b) C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 substituents, where said substituents are selected from: fluoro, C₁₋₃alkoxy, hydroxy, -COR¹¹,
- 30 (c) COR¹¹,
- (d) hydroxy, and
- (e) -O-C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 substituents, where said substituents are selected from: fluoro, C₁₋₃alkoxy, hydroxy, -COR¹¹,
- 35

or R¹⁶ and R¹⁷ are joined together by a C₁₋₄alkyl chain or a C₀₋₃alkyl-O-C₀₋₃alkyl chain to form a 3-6 membered ring;

40 R¹⁸ is selected from:

- 5 (a) hydrogen, and
 (b) C₁₋₆alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,
 (c) fluoro,
 (d) -O-C₃₋₆cycloalkyl, and
 (e) -O-C₁₋₃alkyl, where alkyl is unsubstituted or substituted with 1-6 fluoro,

10 or R¹⁶ and R¹⁸ are joined together by a C₂₋₃alkyl chain to form a 5-6 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -COR¹¹, C₁₋₃alkyl, and C₁₋₃alkoxy,

15 or R¹⁶ and R¹⁸ are joined together by a C₁₋₂alkyl-O-C₁₋₂alkyl chain to form a 6-8 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -COR¹¹, C₁₋₃alkyl, and C₁₋₃alkoxy,

20 or R¹⁶ and R¹⁸ are joined together by a -O-C₁₋₂alkyl-O-chain to form a 6-7 membered ring, where the alkyl are unsubstituted or substituted with 1-3 substituents where the substituents are independently selected from: halo, hydroxy, -COR¹¹, C₁₋₃alkyl, and C₁₋₃alkoxy;

25 R¹⁹ is selected from:

- 30 (a) hydrogen,
 (b) phenyl,
 (c) C₁₋₆alkyl which is substituted or unsubstituted with 1-6 of the following substituents: -COR¹¹, hydroxy, fluoro, chloro, -O-C₁₋₃alkyl;

or R² and R¹⁹ are joined together to form a heterocycle ring with a linker selected from:

- 35 (a) -CH₂(CR²⁸R²⁸)₁₋₃-,
 (b) -CH₂NR²⁹-,
 (c) -NR²⁹CR²⁸R²⁸-,
 (d) -CH₂O-,
 (e) -CH₂SO₂-,
 (f) -CH₂SO-,
 40 (g) -CH₂S-,

(h) -CR²⁸R²⁸-,

where R²⁸ is selected from selected from:

- 5 (a) hydrogen,
- (b) hydroxy,
- (c) halo,
- (d) C₁₋₃alkyl, where the alkyl is unsubstituted or substituted with 1-6 substituents independently selected from: fluoro, and hydroxy,
- 10 (e) -NR¹²R¹²,
- (f) -COR¹¹,
- (g) -CONR¹²R¹²,
- (h) -NR¹²COR¹³,
- (i) -OCONR¹²R¹²,
- 15 (j) -NR¹²CONR¹²R¹²,
- (k) -heterocycle,
- (l) -CN,
- (m) -NR¹²-SO₂-NR¹²R¹²,
- (n) -NR¹²-SO₂-R¹⁴,
- 20 (o) -SO₂-NR¹²R¹², and
- (p) =O, where R²⁸ is connected to the ring via a double bond and the other R²⁸ at the same position is nothing, and

25 where R²⁹ is selected from: hydrogen, C₁₋₃alkyl, where the alkyl is unsubstituted or substituted with 1-6 substituents independently selected from: fluoro, hydroxy, COR¹³, SO₂R¹⁴, and SO₂NR¹²R¹²;

R²⁵ and R²⁶ are independently selected from:

- 30 (a) =O, where R²⁵ and/or R²⁶ is oxygen and is connected via a double bond,
- (b) hydrogen,
- (c) phenyl,
- (d) C₁₋₆alkyl which is substituted or unsubstituted with 1-6 of the following substituents: -COR¹¹, hydroxy, fluoro, chloro, -O-C₁₋₃alkyl;
- 35

m is selected from 0, 1, or 2;

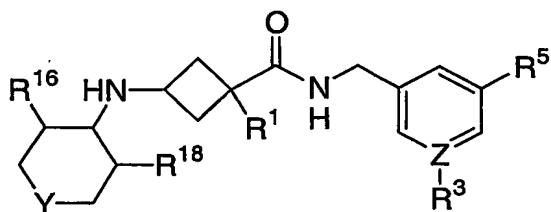
n is selected from 1 or 2;

40 the dashed line represents a single or a double bond;

and pharmaceutically acceptable salts thereof and individual diastereomers thereof.

2. A compound of Claim 1 of formula Ia:

5



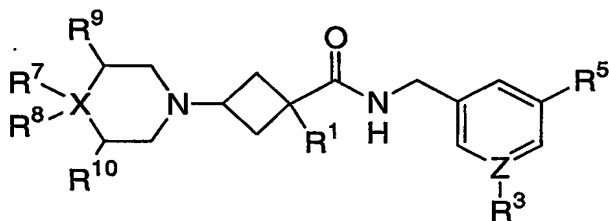
Ia

wherein R¹, R³, R⁵, R¹⁶, R¹⁷, Y, and Z are defined in Claim 1,

10

and pharmaceutically acceptable salts and individual diastereomers thereof.

3. A compound of Claim 1 of formula IIa:



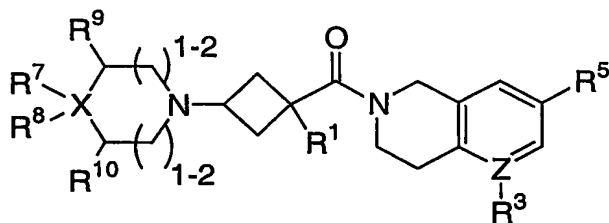
IIa

wherein R¹, R⁵, R⁷, R⁸, R⁹, R¹⁰, X and Z are described in Claim 1, and pharmaceutically acceptable salts and individual diastereomers thereof.

15

4. A compound of Claim 1 of formula IIb:

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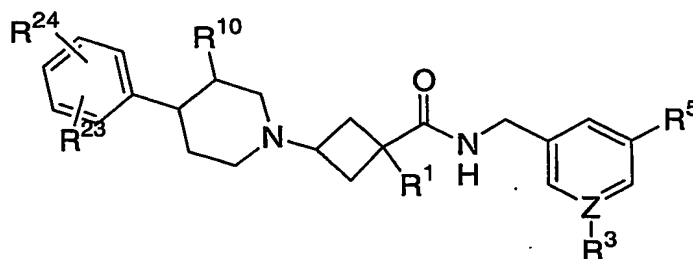
IIb

wherein R¹, R³, R⁵, R⁷, R⁸, R⁹, R¹⁰, X, and Z are defined in Claim 1,

and pharmaceutically acceptable salts and individual diastereomers thereof.

5. A compound of Claim 1 of formula IIc:

5



IIc

wherein R¹, R³, R⁵, R¹⁰, and Z are described in Claim 1, and R²³ and R²⁴ are independently selected from:

10

- (a) hydrogen,
- (b) halo,
- (c) trifluoromethyl,
- (d) hydroxy,
- (e) C₁₋₃alkyl,
- (f) -O-C₁₋₃alkyl,
- (g) -C₀₋₃-CO₂H,
- (h) -C₀₋₃-CO₂C₁₋₃alkyl,
- (i) -CN, and
- (j) -C₀₋₃-heterocycle,

15

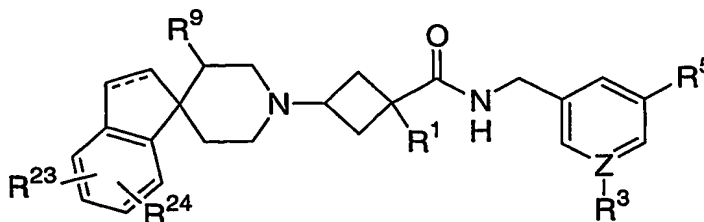
20

or where the R²³ and R²⁴ are joined together to form a heterocycle which is fused to the phenyl ring, and which itself is unsubstituted or substituted with 1-2 substituents independently selected from hydroxy, halo, -COR¹¹, and -C₁₋₃alkyl;

25

and pharmaceutically acceptable salts and individual diastereomers thereof.

6. A compound of Claim 1 of formula IIId:



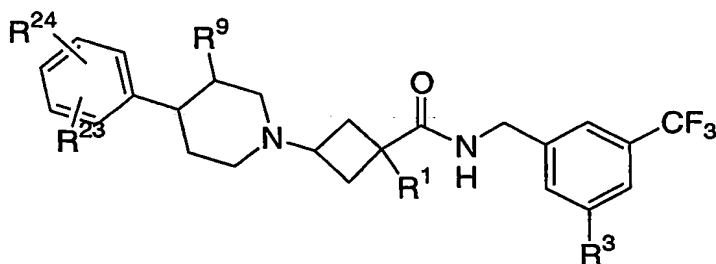
IIId

wherein R¹, R³, R⁵, R⁹, R²³, R²⁴, and Z are defined in Claim 1 and the dashed line represents a single or a double bond,

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and pharmaceutically acceptable salts and individual diastereomers thereof.

7. A compound of Claim 1 of formula IIe:

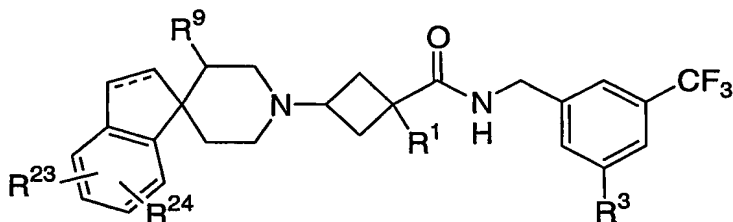


10

IIe

wherein R¹, R³, R⁵, R¹⁰, R²³, and R²⁴ are described in Claim 1, and pharmaceutically acceptable salts and individual diastereomers thereof.

15 8. A compound of Claim 1 of formula IIIf:



IIIf

wherein R¹, R³, R⁵, R⁹, R²³, and R²⁴ are defined in Claim 1,

20

and pharmaceutically acceptable salts and individual diastereomers thereof.

9. A compound of Claim 8 wherein R¹ is selected from:
hydrogen, phenyl, heterocycle, -C₁₋₆alkyl, -C₀₋₆alkyl-O-C₁₋₆alkyl,
and
-(C₀₋₆alkyl)-(C₃₋₇cycloalkyl)-(C₀₋₆alkyl),

25

where said alkyl, phenyl, heterocycle, and cycloalkyl are unsubstituted or substituted with 1-7 substituents, where said substituents are independently selected from:

- (a) halo,
 - (b) hydroxy,
 - (c) -O-C₁₋₃alkyl,
 - (d) trifluoromethyl,
 - (f) C₁₋₃alkyl,
 - (g) -O-C₁₋₃alkyl,
 - (h) -COR¹¹,
 - (i) -CN,
 - (j) -NR¹²R¹², and
 - (k) -CONR¹²R¹².
10. A compound of Claim 9 wherein R¹ is selected from:
- (1) -C₁₋₆alkyl, which is unsubstituted or substituted with 1-6 substituents where said substituents are independently selected from:
 - (a) halo,
 - (b) hydroxy,
 - (c) -O-C₁₋₃alkyl,
 - (d) trifluoromethyl, and
 - (e) -COR¹¹,
 - (2) -C₀₋₆alkyl-O-C₁₋₆alkyl-, which is unsubstituted or substituted with 1-6 substituents where said substituents are independently selected from:
 - (a) halo,
 - (b) trifluoromethyl, and
 - (c) -COR¹¹,
 - (3) -(C₃₋₅cycloalkyl)-(C₀₋₆alkyl), which is unsubstituted or substituted with 1-7 substituents where said substituents are independently selected from:
 - (a) halo,
 - (b) hydroxy,
 - (c) -O-C₁₋₃alkyl,
 - (d) trifluoromethyl, and
 - (e) -COR¹¹,
 - (4) phenyl or heterocycle which is unsubstituted or substituted with 1-3 substituents where said substituents are independently selected from:
 - (a) halo,
 - (b) hydroxy,
 - (c) -O-C₁₋₃alkyl,
 - (d) trifluoromethyl, and
 - (e) -COR¹¹.

11. A compound of Claim 10 wherein R¹ is selected from:
(a) hydrogen,
(b) C₁₋₆alkyl, which is unsubstituted or substituted with 1-6 substituents independently selected from: fluoro and hydroxy
5 (c) phenyl, and
(d) pyridyl.
12. A compound of Claim 6 wherein Z is C and R³ is selected from:
10 (a) hydrogen
(b) halo
(c) hydroxy
(d) C₁₋₃alkyl, where the alkyl is unsubstituted or substituted with 1-6 substituents independently selected from: fluoro, and
15 hydroxy,
(e) -COR¹¹,
(f) -CONR¹²R¹²,
(g) -heterocycle,
(h) -NR¹²-SO₂-NR¹²R¹²,
20 (i) -NR¹²-SO₂-R¹⁴,
(j) -SO₂-NR¹²R¹²,
(k) -nitro, and
(l) -NR¹²R¹².
- 25 13. A compound of Claim 12 wherein Z is C, R³ is selected from:
(a) fluoro,
(b) trifluoromethyl,
(c) hydrogen.
- 30 14. A compound of Claim 8 wherein R⁵ is selected from:
(a) C₁₋₆alkyl substituted with 1-6 fluoro,
(b) -O-C₁₋₆alkyl substituted with 1-6 fluoro,
(c) chloro,
(d) bromo, and
35 (e) phenyl.
15. A compound of Claim 4 wherein R⁷ is phenyl, heterocycle, C₃₋₇cycloalkyl, C₁₋₆alkyl, -COR¹¹, and -CONH-V-COR¹¹,
40 where V is selected from C₁₋₆alkyl or phenyl, and

where the phenyl, heterocycle, C₃₋₇cycloalkyl, and C₁₋₆alkyl is unsubstituted or substituted with 1-5 substituents, where said substituents are independently selected from:

- 5 (a) halo,
(b) trifluoromethyl,
(c) hydroxy,
(d) C₁₋₃alkyl,
(e) -O-C₁₋₃alkyl,
10 (f) -COR¹¹,
(g) -CN,
(h) -heterocycle, and
(i) -CONR¹²R¹².

16. A compound of Claim 15 wherein, when X is not O, R⁷ is phenyl,
15 heterocycle, C₁₋₄alkyl, -COR¹¹ or -CONH-V-COR¹¹;
V is selected from C₁₋₆alkyl or phenyl; and
the phenyl, heterocycle, and C₁₋₄alkyl is unsubstituted or substituted
with 1-3 substituents, where said substituents are independently
selected from:

- 20 (a) halo,
(b) hydroxy,
(c) C₁₋₃alkyl,
(d) -O-C₁₋₃alkyl,
(e) -COR¹¹, and
25 (f) -heterocycle.

17. A compound of Claim 7 wherein R¹⁰ is selected from:
(a) hydrogen,
(b) hydroxy,
30 (c) -CH₃,
(d) -O-CH₃, and
(e) =O (where R⁹ is joined to the ring via a double bond).

- 35 18. A compound of Claim 2 wherein R¹⁶ is selected from:
(a) hydrogen,
(b) C₁₋₃alkyl, which is unsubstituted or substituted with 1-6
fluoro,
(c) -O-C₁₋₃alkyl,
40 (d) fluoro, and
(e) hydroxy.

19. A compound of Claim 18 wherein R¹⁶ is selected from:
- (a) hydrogen,
 - (d) trifluoromethyl,
 - (c) methyl,
 - 5 (d) methoxy,
 - (e) ethoxy,
 - (f) ethyl,
 - (g) fluoro, and
 - 10 (h) hydroxy.
20. A pharmaceutical composition which comprises an inert carrier and a compound of Claim 1.
- 15 21. A method for modulation of chemokine receptor activity in a mammal which comprises the administration of an effective amount of a compound of Claim 1.
22. A method for treating, ameliorating, controlling or reducing the risk of an inflammatory and immunoregulatory disorder or disease which comprises the
- 20 administration to a patient of an effective amount of a compound of Claim 1.
23. A method for treating, ameliorating, controlling or reducing the risk of rheumatoid arthritis which comprises the administration to a patient of an effective amount of a compound of Claim 1.